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(54) **Vacuum filter device**

Vakuumfiltervorrichtung

Dispositif de filtrage à vide

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(73) Proprietor: **MILLIPORE CORPORATION**
Billerica, Massachusetts 01821 (US)

(72) Inventors:
- **Clark, Phillip**
  Wakefield, MA 01880 (US)
- **Foley, Brian D.**
  Westford, MA 01886 (US)
- **Pitt, Aldo M.**
  Wayland, MA 01778 (US)

(74) Representative: **Henkel, Feiler & Hänzel**
Möhlstrasse 37
81675 München (DE)

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Description

BACKGROUND OF THE INVENTION

[0001] The present invention generally relates to vacuum filter devices and particularly to such devices for filtering liquids from one container through a membrane and depositing the filtrate directly into another container. More particularly, the invention relates to a liquid-tight filtration system in which solutions, such as tissue culture media, are vacuum filtered.

[0002] Devices for filtering biological solutions generally involve three primary components, i.e. a membrane filter interposed between two vessels, a feed container located upstream of the membrane for holding the sample solution to be filtered and a filtrate container located downstream of the membrane filter for collecting the filtered sample solution. Often a vacuum is drawn downstream of the membrane to increase the rate of filtration by creating a pressure differential across the filter. However, in such cases provisions must be made to maintain the pressure differential across the membrane and thus assuring that the filtration will not stop.

[0003] The arrangement of the components for vacuum filtration can take various forms; however, especially in laboratory settings, ease of use, reduced storage requirements and minimal disposable hardware are important concerns as is avoiding spillage of the biological solution. In certain other applications, preserving the sterility of the solution being filtered is also important.

[0004] US-A-4,251,366 discloses an adapter to be utilized to effect fluid communication between a conventional laboratory vessel having a threaded neck and a sample container. The adapter is threadably mounted on the vessel. The sample container, housing a sample, is mounted on the adapter such that a filtration membrane is interposed between the sample container and the laboratory vessel which accepts and houses a filtrate produced by filtering the sample through the membrane. A means for effecting a vacuum between the sample container and the laboratory vessel provides a means for effecting vacuum filtration of the sample. No means are provided for maintaining a pressure differential across the membrane so that a high flow rate through the filter can be maintained.

[0005] An example of a vacuum filter device is described in US-A-4,673,501 wherein an open funnel for receiving a sample of solution to be filtered is arranged to be sealed to the top of a bottle for collecting filtrate. The base of the funnel includes a membrane filter positioned such that when the sample to be filtered is poured into the top of the funnel all of the sample solution is directed to flow through the membrane filter. A vacuum conduit which is adapted to be connected to a vacuum source is formed within the base of the funnel and allows a vacuum to be drawn within the filtrate bottle thereby drawing the sample solution through the membrane filter. Since the pressure differential across the filter is constant due to the application of a vacuum on the downstream side of the filter and atmospheric pressure present on the liquid surface of the open funnel, rapid filtration is possible and any reduction in flow rate is due to filter fouling. Nonetheless, vacuum filter devices of the type described in this patent suffer from a number of drawbacks which make them inconvenient for laboratory use. First, these devices require the liquid sample be transferred from its normal laboratory container to an open funnel. Because of the liquid weight concentrated at the top of this assembly, they are prone to tipping and hence spilling the biological solution during pouring of sample or when connecting hoses. Aside from the inconvenience to the user in handling the fluid to be filtered, there is an enhanced risk of compromising the sterility of the particular biological solution due to the open nature of this device. Moreover, the large size of these filter assemblies results in their taking up limited laboratory storage space. In addition, since the containers utilized in the filtration process are disposable and intended for one-time use, a significant amount of solid waste is generated by these filter assemblies and the associated pre-and post-filtration containers.

[0006] To minimize the amount of solid waste and fluid transfers, US-A-5,141,639 describes a vacuum filter assembly wherein the membrane filter is disposed in a cover sealable to the filtrate container. The cover is formed with a feed port in the form of a tubular feed nipple on the upstream side of the membrane filter. A length of tubing is connected at one end to the feed nipple and the other end is directly inserted into a sample container housing the solution to be filtered. The cover also includes a filtrate outlet port and a vacuum port, both of which fluidically connect with the downstream side of the membrane filter. When tubing is attached to the vacuum port and a vacuum is drawn the sample solution to be filtered is caused to flow through the tubing and pass through the membrane filter to the filtrate container. As is the case with the aforementioned US-A-4,673,501, the pressure difference in this prior art assembly remains constant because of the vacuum in the filtrate container and the atmospheric pressure acting on the liquid surface in the open feed or sample container. While this device minimizes the amount of solid waste generated during filtration, it is cumbersome to use as the operator must assemble the tubing to the cover and hold the cover on the filtrate container until the necessary vacuum pressure has been achieved in the filtrate container. Additionally, the feed tubing must be maintained submerged in the sample container to avoid air being drawn into the sample solution which could disrupt the filtration. In addition, the sample is housed in an open container; therefore; the risk of compromising sterility is heightened.

[0007] Thus it is apparent that the need still exists for an improved vacuum filter device that is easy to use, reduces the solid waste generated, minimizes the number of times the fluid is transferred and reduces the

risk of liquid spillage.

SUMMARY OF THE INVENTION

[0008] The present invention overcomes the disadvantages and limitations of the prior art by providing a vacuum filter device for filtering solutions which includes the features of claim 1. Specifically, the filter device comprises a filter body having two junctions disposed on opposite sides of a filter. Each junction is adapted to receive a closed container in a fluid-tight, sealed relationship. Other aspects of the invention include provisions for forming a substantially liquid-tight filtration system and for reducing the risk of contaminating the sample solution to be filtered. The invention also minimizes the risk of spillage and contamination of the solution by eliminating fluid transfer between open containers. The device also includes a vacuum port communicating with the downstream side of the filter, and hence the filtrate container. When connected to a vacuum source, the pressure differential will allow a vacuum to draw the sample solution from the sample container through the filter and into the filtrate container. To maintain the pressure differential necessary to continue the flow of sample, a passageway communicates with the upstream side of the membrane, and hence the sample container, to provide a vent to atmospheric pressure.

[0009] In accordance with a preferred embodiment of the invention, two identical laboratory containers, for example centrifuge tubes, are screwed onto opposite sides of a filter body. The filter body has two mating threaded recesses disposed along the central axis of the body, with each recess having a raised annular ring for creating a fluid-tight seal with the top of the container when it is screwed into the body. The portion of the filter body between the two recesses includes a membrane filter bonded to a suitable support. Two passageways formed in the filter body communicate fluidically with the opposite sides of the membrane and ultimately with each of the containers. One of the passageways is a vacuum port which communicates with the downstream side of the membrane and is adapted to be connected to a vacuum source for enabling sample to be drawn through the membrane filter and be collected as filtrate. The other passageway communicates with the upstream side of the membrane (and the sample container) and serves as a vent to atmospheric pressure. This vent passageway is sealed by a hydrophobic membrane. When a sample solution is placed in the sample container and both the sample container and an empty filtrate container are secured to the filter body, a vacuum is applied to the vacuum port to create a pressure differential between the two containers. This pressure differential causes sample fluid to pass through the membrane filter from the sample container to the filtrate container. As the volume of fluid in the sample container is reduced, air enters through the venting passageway to maintain the pressure differential across the membrane so that filtration continues uninterrupted until all the sample is filtered.

[0010] These and other aspects and advantages of the invention will become apparent from the following detailed description taken in conjunction with the drawings.

DESCRIPTION OF THE DRAWINGS

[0011]

Fig. 1 is a front elevation view of a preferred embodiment of a vacuum filter device with laboratory containers coupled thereto in accordance with the invention;

Fig. 2 is a detailed sectional view of a filter body similar to that of the device of Fig. 1 for explaining certain features common with the invention;

Fig. 3 is an exploded view of the filter body illustrating the assembly of the membrane filter;

Figs. 4A, B and C are a series of diagrammatic views illustrating the process of forming the venting passageway in the device of Fig. 2;

Fig. 5 is a sectional view of an embodiment of a vacuum filter device in accordance with the invention; and

Fig. 6 is a sectional view of an alternate embodiment of a vacuum filter device in accordance with the invention.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[0012] Fig. 1 shows a vacuum filter device **10** which includes a filter body generally indicated by numeral **11** having a pair of axially disposed tubular holders **12, 13** each having a threaded open end. The holders are bonded back-to-back (see also Fig. 3) at interface **14** by any suitable welding technique such as ultrasonic welding to form an integral body. The open ends of the holders serve as a junction to accept a closed sample container **15** for a biological fluid such as tissue culture media to be filtered and a closed filtrate container **16** for collecting the filtered sample (filtrate).

[0013] The holder **13** includes a face plate **17** with a series of radially extending ribs **19** molded on the top surface of the plate which act as a support for a porous membrane **18** which is welded at its periphery to the plate **17** prior to bonding the two holders together. For applications involving the sterile filtration of tissue culture media, a particularly suitable microporous membrane is a 0.22 µm (0.22 micron) polyethersulfone membrane available from Millipore Corporation under the brand name Express™. However, depending on the filtration application, the membrane may be made from any other suitable polymeric materials such as mixed esters of cellulose, cellulose acetate, polycarbonate, polyvinylidene fluoride, polytetrafluoroethylene, nylon,

polypropylene, polyethylene or the like. The use of inorganic materials is also possible as well as filter structures that are not microporous (e.g. depth filters). In some applications, a combination of filters may provide improved performance. For example, for particularly dirty samples a depth filter in combination with a microporous membrane filter can be used.

[0014] Referring also to Fig. 2, the bottom of the holder **12** which abuts the face plate **17** includes a membrane guard **20** formed as part of the holder. The guard is wagon-wheeled shaped such that when the two holders **12, 13** are bonded together sample solution can flow through a series of openings **21** and then be filtered by the membrane **18.** A passageway **30** provides the fluid communication link between the downstream side of the membrane **18** and the filtrate container **16.**

[0015] The filter body **11** has respective raised annular rings **22A, 22B** which are molded within each of the holders **12, 13** near to their periphery. A vacuum port **23** in communication with the downstream side of the membrane **18** includes a filter matrix **24** within the central bore of the port **23.** The matrix **24** is used to prevent the migration of contaminants such as bacteria or oil residues from entering the filtrate during vacuum operation as well as to protect the vacuum system from being contaminated by the filtered sample. A tube adapter **26** is secured to the vacuum port. A venting passageway **25** is formed at the interface **14** of the two holders and is in fluid communication with the upstream side of the membrane and provides a vent for the sample container **15.**

[0016] The inclusion of the venting passageway **25** is important to the proper operation of the vacuum filter device **10** because the sample container **15** is a closed vessel and the overall filter device is of liquid-tight construction. The venting passageway allows for maintaining the necessary pressure differential across the filter, a feature attributed to the previously described prior art because of the open nature of their feed containers at a sacrifice of the benefits of the liquid-tight system of the present embodiment, such as minimizing the risk of spills and contamination. While a closed sample container would be able to start the filtration process, it would not provide commercially acceptable performance over the course of filtration. To explain, the closed sample container starts the filtration process with an internal starting pressure at atmospheric pressure. As vacuum is applied to the vacuum port **23**, the pressure differential (ΔP) across the membrane is defined by $\Delta P = (P_{sample} - P_{filtrate})$ where P_{sample} is the air pressure in the sample container and $P_{filtrate}$ is the air pressure in the filtrate container. Initially, $P_{sample} = P_{filtrate} = P_{atmosphere}$; however, as fluid is drawn through the membrane **18** to the filtrate container **16** the sample volume is being reduced. In a closed system, this reduction in the amount of sample in the sample container over time t_1 to t_2 translates to a reduction in pressure, as governed by the pressure/volume relationship ($P_{sample(t1)}$ $V_{sample(t1)}$ = $P_{sample(t2)}$ $V_{sample(t2)}$) where P_{sample} and V_{sample} relate to the gas within the sample container. As the pressure in the sample container is reduced, the ΔP is lessened thereby slowing the flow rate. If allowed to continue P_{sample} will equal $P_{filtrate}$ resulting in no flow. To insure the maximum ΔP and hence the greatest flow rate, the sample container needs to be maintained as close to $P_{atmosphere}$ as possible. With the present invention, this goal is achieved by the venting passageway sealed by a hydrophobic membrane connecting the sample container with the outside atmospheric pressure.

[0017] Details of the techniques used to create this small dimension passageway in the filter body **11** are best discussed with reference to Figs. 4A, B and C. As discussed, the filter body is constructed by ultrasonically welding the two holders **12, 13** at the interface **14.** As shown in Fig. 4A, a forming tool **50** is placed between the two holders prior to initiating the weld process. This tool can take a variety of shapes depending on the desired dimensions of the orifice. In this embodiment a circular wire of diameter 0.381 mm (0.015 inches) is used, although it will be understood that forms of rectangular cross-section or even other geometries may be employed. Fig. 4B shows the holders placed together with the forming tool in position as ultrasonic energy is applied. After the holders are welded together, the forming tool is removed leaving a through-hole whose dimensions correspond to that of the tool. To assist in the removal, the remote end of the forming tool can be slightly tapered such that as the minimum force required to begin disengaging the forming tool is applied the remainder of the tool will more readily be removed from the interface **14** between the two holders.

[0018] Injection molding methods generally provide the greatest dimensional control of shape with plastic parts. To apply conventional molding techniques in the present instance, it would be desirable to mold a passageway in the wall section of the filter body **11** remote from the joining surfaces of the two holders **12, 13** in order to eliminate the deformation of the passageway during assembly thereby retaining the dimensional control. However, conventional molding processing techniques would not allow a passageway that is molded into the wall of the holder **12** to be 0.381 mm (0.015 inches) or less. This is because as the molten plastic enters the mold cavity the pin used to create the passageway would deflect leading to fatigue and breakage. Also, for the pin to seal off against the other wall of the cavity, the sealing end of the pin will be peened over in time leading to flashing. Flashing is an uncontrollable, undesirable migration of plastic, which in this example will lead to filling and dimensionally distorting the venting passageway 25.

[0019] If, instead of molding a passageway in the wall of the filter body **11** as discussed above, an attempt were made to mold an interruption or notch on the joining surfaces of the holders **12, 13** with dimensions of 0.381mm (0.015 inches)or less, the joining process,

whether it be vibrational, thermal or chemical, would distort or even close the passageway because the two surfaces are joined by softening and moving the plastic together followed by a stabilization period. The plastic that moves during joining will be squeezed into available areas, such as the void created by the molded in interruption. Also the direction of movement of the plastic during the joining process is not controllable. Thus as the plastic moves into the interruption it will dimensionally change the shape and possibly close the interruption altogether.

[0020] The use of a forming tool during the joining process provides for a dimensionally controlled geometry that is independent of the molding process and controllable with a variety of joining processes in addition to the ultrasonic welding process of the embodiment described, such as vibration bonding, radiant heat and other fusion bonding processes as well as solvent bonding.

[0021] In operation, a sample solution to be filtered is deposited in the sample container **15** and is screwed tightly onto the holder **12** with the open end of the sample container being held upward until the upper lip of the container is squeezed against the angled surface of the ring **22A.** Tightly screwing the container to the filter body **11** creates a fluid-tight seal. In similar fashion, the filtrate container **16** is screwed into the holder **13** against the angled surface of the ring **22B**. For sterile filtration of tissue culture, the filtrate container and the filter body are pre-sterilized prior to coupling them together.

[0022] The device **10** is then flipped over such that the sample container **15** is oriented upward with respect to the filter body **11** as shown in Fig. 1. A length of tubing **28** is connected to a vacuum pump (not shown) and a vacuum is applied to port **23** and the filtrate container is evacuated of air and the pressure therein correspondingly reduced. The unfiltered sample solution is then passed from the higher pressure sample container **15** through the membrane guard **20** and the membrane **18.** The filtered solution flows through the opening **30** and collects as filtrate in the filtrate container **16**. To maintain the pressure differential, which serves as a driving force, air at atmospheric pressure enters through the venting passageway **25** and replaces the volume of sample solution that passes through the membrane.

[0023] Fig. 5 shows an embodiment of the device **10** in accordance with the invention wherein like numerals refer to the same elements as those shown in Fig. 1. The construction and operation is similar to the Fig. 1 embodiment except the vent for the sample container **15** is a passageway **60** whose dimensions are compatible with those derived from conventional molding techniques (i.e. > 0.381mm (0.015 inches)). In this instance a hydrophobic membrane **62** covers the opening of the passageway **60** to keep sample solution from spilling out of as well as preventing microbes from entering the container **15**. Thus when used with a sterilizing grade filter such as the aforementioned Express™ membrane, the filtration system of this embodiment represents a sterile, closed system which maintains the sterility of the solutions being processed.

[0024] Fig. 6 shows another embodiment similar to that of the Fig. 5 embodiment except that no vent membrane is used to cover passageway **70**. Instead the membrane **18** includes both a hydrophilic region **71** which separates the two closed containers **15, 16** and a hydrophobic region **72** which is in direct fluid communication with the passageway **70**. In this instance the membrane is also sealed to the face plate **17** at bonding point **73** in the vicinity of the interface between the hydrophilic and hydrophobic regions. To assure that the hydrophobic region forms an integral seal with the passageway, the membrane seal at point **73** must straddle both the hydrophilic and hydrophobic regions. As vacuum is drawn through the port **23,** the sample solution will flow through the hydrophilic region of the membrane. At the same time air enters the passageway **70** and ultimately passes into the sample container **15** through the hydrophobic region of the membrane. This embodiment thus presents the same attributes of liquid-tight and sterile sealed filtration as that of the embodiment shown in Fig. 5.

Claims

1. A vacuum filter device comprising:

   a filter body (11) having two junctions (12,13) disposed from one another, each of said junctions (12,13) being adapted to receive respective feed and filtrate containers (15,16);
   each of said junctions (12,13) including sealing means (22A,22B) for creating a liquid tight seal when said containers (15,16) are coupled to said filter body (11), said feed container (15) serving to house a liquid to be filtered and said filtrate container (16) serving to receive the filtered liquid, each of said containers (15,16) forming liquid tight receptacles when coupled to said filter body (11);
   a filter (18) sealed within said filter body (11) between said junctions (12,13) so that liquid in said feed container (15) on an upstream side of said filter (18) must pass through said filter (18) to a downstream side of the filter (18) prior to entering said filtrate container (16);
   a vacuum port (23) extending through said filter body (11) and being in fluid communication with said downstream side of said filter (18), said vacuum port (23) being adapted to be connected to a vacuum source for drawing said liquid from said upstream side of the filter (18), through said filter (18) and to said downstream side of the filter (18);

   characterized in that

a vent passageway (60;70) is formed in said filter body (11) communicating with the upstream side of said filter (18) and with the atmosphere surrounding said vacuum filter device (10), said vent passageway (60;70) being sealed by a hydrophobic membrane (62;72) such that the passage of liquid from the upstream side of the filter to the atmosphere is prevented during normal use while gas from the atmosphere can pass to the upstream side of the filter (18).

2. The device of claim 1 wherein said filter (18) is a microporous membrane.

3. The device of claim 1 or 2 wherein said filter (18) is a depth filter.

4. The device of any one of claims 1 to 3 wherein said filter (18) is a combination of a microporous membrane and a depth filter.

5. The device of any one of claims 1 to 4 wherein said hydrophic membrane (62;72) integrally seals said vent passageway (60;70).

6. The device of any one of claims 1 to 5 wherein said filter (18) is segmented into hydrophilic (71) and hydrophobic regions (72).

7. The device of claim 6 wherein said hydrophilic region (71) separates said feed and filtrate containers (15,16) and hydrophobic region (72) integrally seals said vent passageway (70).

8. The device of any one of claims 1 to 7 wherein said filter body (11) is of circular cross-section, said junctions are threaded holders (12,13) axially disposed from each other and adapted to mate and engage with threads provided on said feed and filtrate containers (15,16).

9. The device of claim 8 wherein said sealing means comprises a raised annular ring (22A,22B) adapted to engage said feed and filtrate containers (15,16) to form a compressive fit between said ring (22A, 22B) and a wall of said holders (12,13) when said feed and filtrate containers (15,16) are threaded into the threads of said holders (12,13).

10. The device of any one of claims 1 to 9 wherein said sealing means comprises an elastomeric gasket positioned within a base of said holders (12,13).

11. The device of any one of claims 1 to 10 including a prefilter matrix disposed upstream of said filter (18).

Patentansprüche

1. Unterdruckfiltervorrichtung mit:

einem Filterkörper (11) mit zwei Verbindungsstellen (12,13), die entfernt voneinander angeordnet sind, wobei jede der Verbindungsstellen (12,13) betreffende Zustrom- und Filtratbehälter (15,16) aufzunehmen vermag,

wobei jede der Verbindungsstellen (12,13) Dichtungsmittel (22A,22B) zum Erzeugen einer flüssigkeitsdichten Dichtung, wenn die Behälter (15,16) mit dem Filterkörper (11) gekoppelt sind, aufweist, wobei der Zustrombehälter (15) dazu dient, eine zu filternde Flüssigkeit aufzunehmen und der Filtratbehälter (16) dazu dient, die gefilterte Flüssigkeit aufzunehmen, wobei jeder der Behälter (15,16) flüssigkeitsdichte Aufnahmen bildet, wenn er mit dem Filterkörper (11) gekoppelt ist,

einem Filter (18), der in dem Filterkörper (11) zwischen den Verbindungsstellen (12,13) derart dicht aufgenommen ist, daß Flüssigkeit in dem Zustrombehälter (15) auf einer stromaufwärtigen Seite des Filters (18) durch das Filter (18) zu einer stromabwärtigen Seite des Filters (18) vor dem Eintritt in den Filtratbehälter (16) durchlaufen muss,

einem Unterdruckanschluß (23), der sich durch den Filterkörper (11) erstreckt und in Fluidverbindung mit der stromabwärtigen Seite des Filters (18) steht, wobei der Unterdruckanschluß (23) mit einer Unterdruckquelle verbunden zu werden vermag, um die Flüssigkeit von der stromaufwärtigen Seite des Filters (18) durch das Filter (18) zu der stromabwärtigen Seite des Filters (18) zu saugen,

dadurch gekennzeichnet, daß

ein Be- bzw. Entlüftungsdurchgang (60;70) in dem Filterkörper (11) ausgebildet ist, der mit der stromaufwärtigen Seite des Filters (18) und mit der die Unterdruckfiltervorrichtung (10) umgebenden Atmosphäre in Verbindung steht, wobei der Be- bzw. Entlüftungsdurchgang (60;70) durch eine hydrophobe Membran (62;72) derart abgedichtet ist, daß das Passieren von Flüssigkeit von der stromaufwärtigen Seite des Filters in die Atmosphäre während einer normalen Verwendung verhindert wird, während Gas von der Atmosphäre zur stromaufwärtigen Seite des Filters (18) passieren kann.

2. Vorrichtung nach Anspruch 1, wobei das Filter (18) eine mikroporöse Membran ist.

3. Vorrichtung nach Anspruch 1 oder 2, wobei das Filter (18) ein Tiefenfilter ist.

4. Vorrichtung nach einem der Ansprüche 1 bis 3, wobei das Filter (18) eine Kombination einer mikropo-

rösen Membran und eines Tiefenfilters ist.

5. Vorrichtung nach einem der Ansprüche 1 bis 4, wobei die hydrophobe Membran.(62;72) den Be- bzw. Entlüftungsdurchgang (60;70) integral abdichtet.

6. Vorrichtung nach einem der Ansprüche 1 bis 5, wobei das Filter (18) in hydrophile (71) und hydrophobe Bereiche (72) segmentiert ist.

7. Vorrichtung nach Anspruch 6, wobei der hydrophile Bereich (71) die Zustrom- und Filtratbehälter (15,16) trennt und der hydrophobe Bereich (72) den Be- bzw. Entlüftungsdurchgang (70) integral abdichtet.

8. Vorrichtung nach einem der Ansprüche 1 bis 7, wobei der Filterkörper (11) von kreisförmigem Querschnitt ist, die Verbindungsstellen mit Gewinde versehene Halteelemente (12,13) sind, die axial voneinander angeordnet und so ausgelegt sind, daß sie in an den Zustrom- und Filtratbehältern (15,16) vorgesehene Gewinde passen und in diese eingreifen.

9. Vorrichtung nach Anspruch 8, wobei das Dichtungsmittel einen erhabenen Ring (22A,22B) umfaßt, der mit den Zustrom- und Filtratbehältern (15,16) in Eingriff zu kommen vermag, um einen Kompressionssitz zwischen dem Ring (22A,22B) und einer Wand der Halteelemente (12,13) zu bilden, wenn die Zustrom- und Filtratbehälter (15,16) in die Gewinde der Halteelemente (12,13) eingeschraubt werden.

10. Vorrichtung nach einem der Ansprüche 1 bis 9, wobei das Dichtungsmittel einen elastomeren Dichtungsring umfaßt, der innerhalb einer Basis der Halteelemente (12,13) positioniert ist.

11. Vorrichtung nach einem der Ansprüche 1 bis 10 mit einer stromaufwärts des Filters (18) angeordneten Vorfiltermatrix.

Revendications

1. Dispositif de filtrage à vide, comprenant :

un corps (11) de filtre comportant deux raccords (12, 13) disposés l'un par rapport à l'autre, chacun desdits raccords (12, 13) étant apte à recevoir des conteneurs respectifs (15, 16) d'alimentation et de filtrat ;
chacun desdits raccords (12, 13) incluant un moyen (22A, 22B) d'étanchéité servant à créer une étanchéité au liquide lorsque lesdits conteneurs (15, 16) sont couplés audit corps (11) de filtre, ledit conteneur (15) d'alimentation servant à contenir un liquide à filtrer et ledit conteneur (16) de filtrat servant à recevoir le liquide filtré, chacun desdits conteneurs (15, 16) formant des réceptacles étanches au liquide lorsqu'ils sont accouplés audit corps (11) filtre ;
un filtre (18) scellé à l'intérieur dudit corps (11) de filtre entre lesdits raccords (12, 13), de sorte que du liquide qui se trouve dans ledit conteneur (15) d'alimentation du côté amont dudit filtre (18) doit passer à travers ledit filtre (18) vers un côté aval du filtre (18) avant de pénétrer ledit conteneur (16) de filtrat ;
un orifice (23) d'établissement de vide s'étendant à travers ledit corps (11) de filtre et étant en communication fluidique avec ledit côté aval dudit filtre (18), ledit orifice (23) d'établissement de vide étant apte à être raccordé à une source de vide dans le but de tirer ledit liquide dudit côté amont du filtre (18), à travers ledit filtre (18) et vers ledit côté aval du filtre (18) ;

caractérisé en ce que
un conduit (60 ; 70) d'évent est formé dans ledit corps (11) de filtre en communication avec le côté amont dudit filtre (18) et avec l'atmosphère qui entoure ledit dispositif (10) de filtrage à vide, ledit conduit (60 ; 70) d'évent étant rendu étanche par une membrane hydrophobe (62 ; 72), de sorte que le passage de liquide du côté amont du filtre vers l'atmosphère ne peut pas se faire pendant une utilisation normale tandis que du gaz provenant de l'atmosphère peut aller vers le côté amont du filtre (18).

2. Dispositif selon la revendication 1, dans lequel ledit filtre (18) est une membrane microporeuse.

3. Dispositif selon la revendication 1 ou 2, dans lequel ledit filtre (18) est un filtre creux.

4. Dispositif selon l'une quelconque des revendications 1 à 3, dans lequel ledit filtre (18) est une combinaison d'une membrane microporeuse et d'un filtre creux.

5. Dispositif selon l'une quelconque des revendications 1 à 4, dans lequel ladite membrane hydrophobe (62 ; 72) assure une étanchéité intégrale dudit conduit (60 ; 70) d'évent.

6. Dispositif selon l'une quelconque des revendications 1 à 5, dans lequel ledit filtre (18) est segmenté en régions hydrophiles (71) et hydrophobes (72).

7. Dispositif selon la revendication 6, dans lequel ladite région hydrophile (71) sépare lesdits conteneurs (15, 16) d'alimentation et de filtrat, et dans lequel ladite région hydrophobe (72) assure une

étanchéité intégrale dudit conduit (70) d'évent.

8. Dispositif selon l'une quelconque des revendications 1 à 7, dans lequel ledit corps (11) de filtre a une section transversale circulaire, lesdits raccords sont des dispositifs de maintien filetés (12, 13) disposés axialement l'un par rapport à l'autre et aptes à s'accoupler et engager avec les filets prévus sur lesdits conteneurs (15, 16) d'alimentation et de filtrat.

9. Dispositif selon la revendication 8, dans lequel ledit moyen d'étanchéité comprend une bague annulaire surélevée (22A, 22B) apte à engager lesdits conteneurs (15, 16) d'alimentation et de filtrat pour former un montage à compression entre ladite bague (22A, 22B) et une paroi desdits dispositifs de maintien (12, 13) lorsque lesdits conteneurs (15, 16) d'alimentation et de filtrat sont vissés dans les filets desdits dispositifs de maintien (12, 13).

10. Dispositif selon l'une quelconque des revendications 1 à 9, dans lequel ledit moyen d'étanchéité comprend une garniture en élastomère placée à l'intérieur d'une base desdits dispositifs de maintien (12, 13).

11. Dispositif selon l'une quelconque des revendications 1 à 10, incluant une matrice de préfiltrage disposée en amont dudit filtre (18).

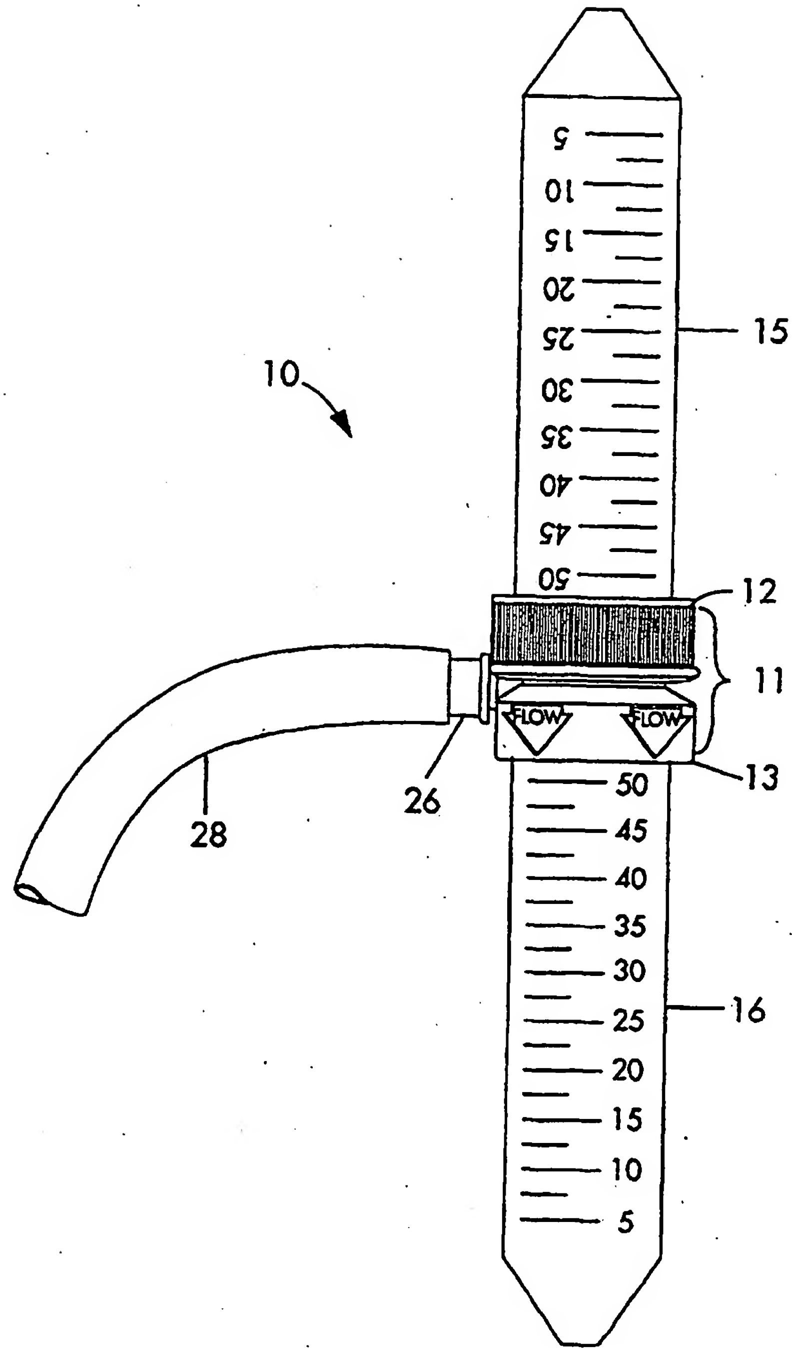
10
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Fig. 1

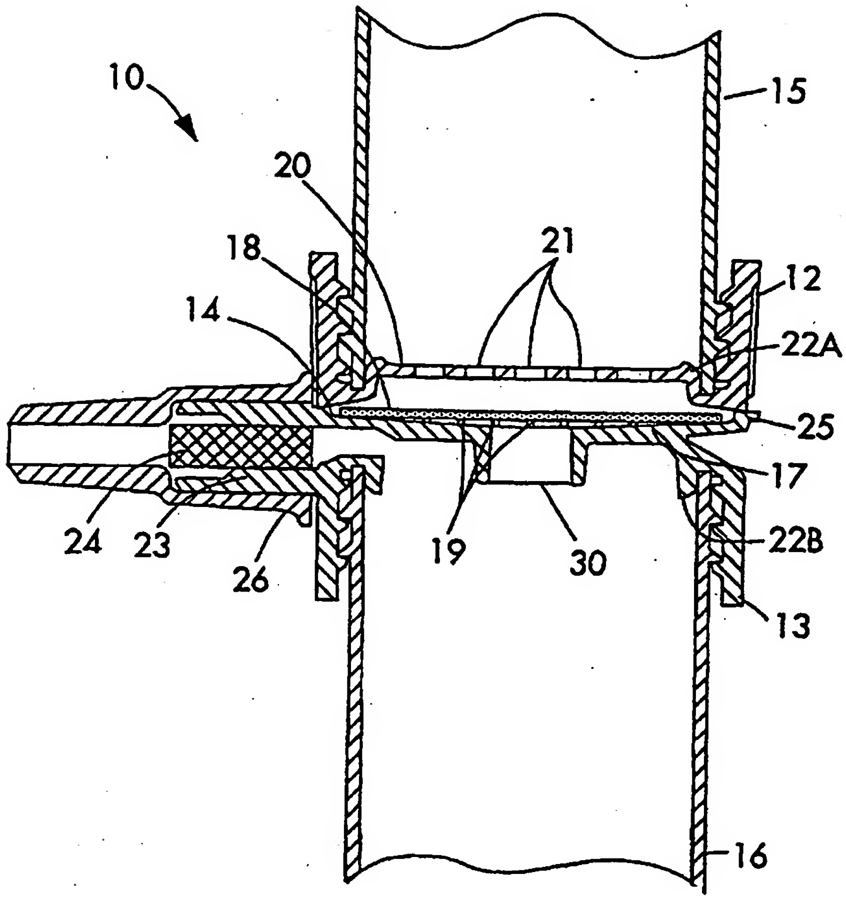

Fig. 2

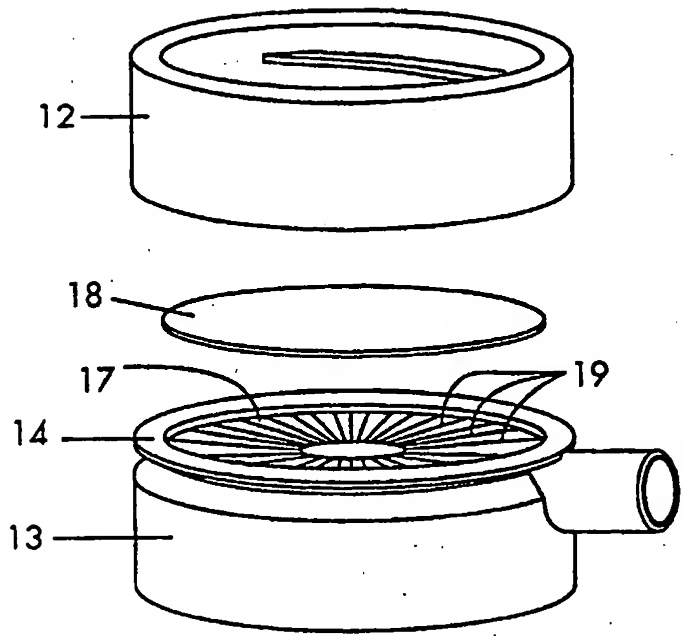

Fig. 3

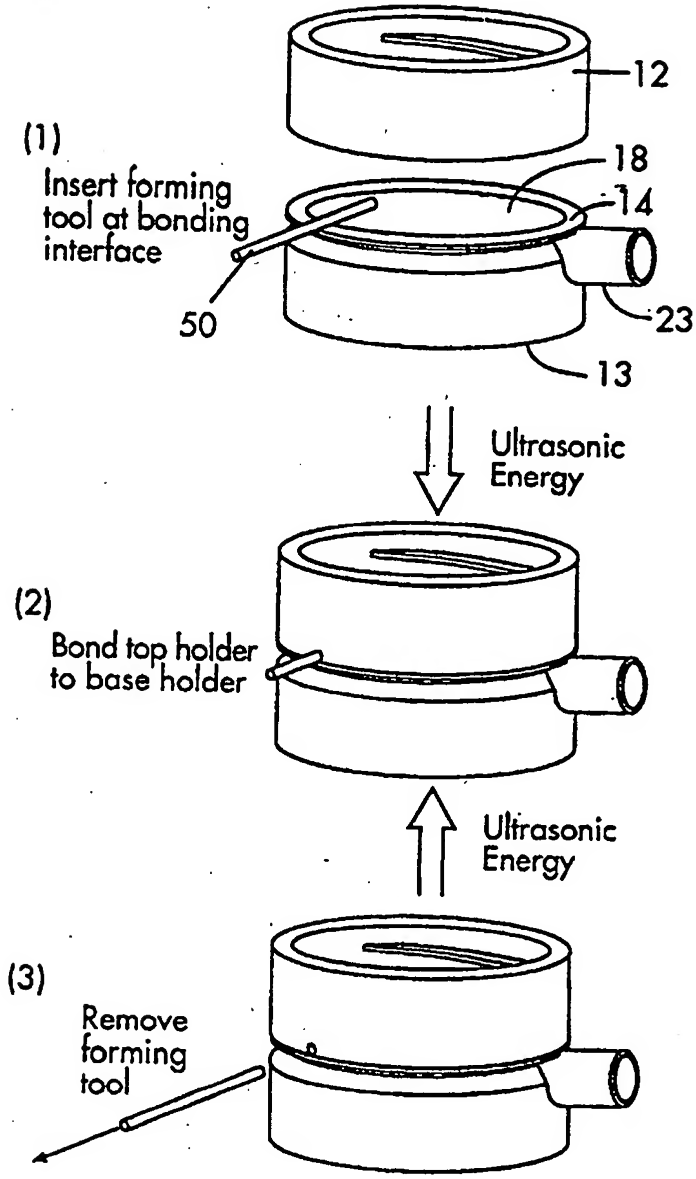

Fig. 4A

Fig. 4B

Fig. 4C

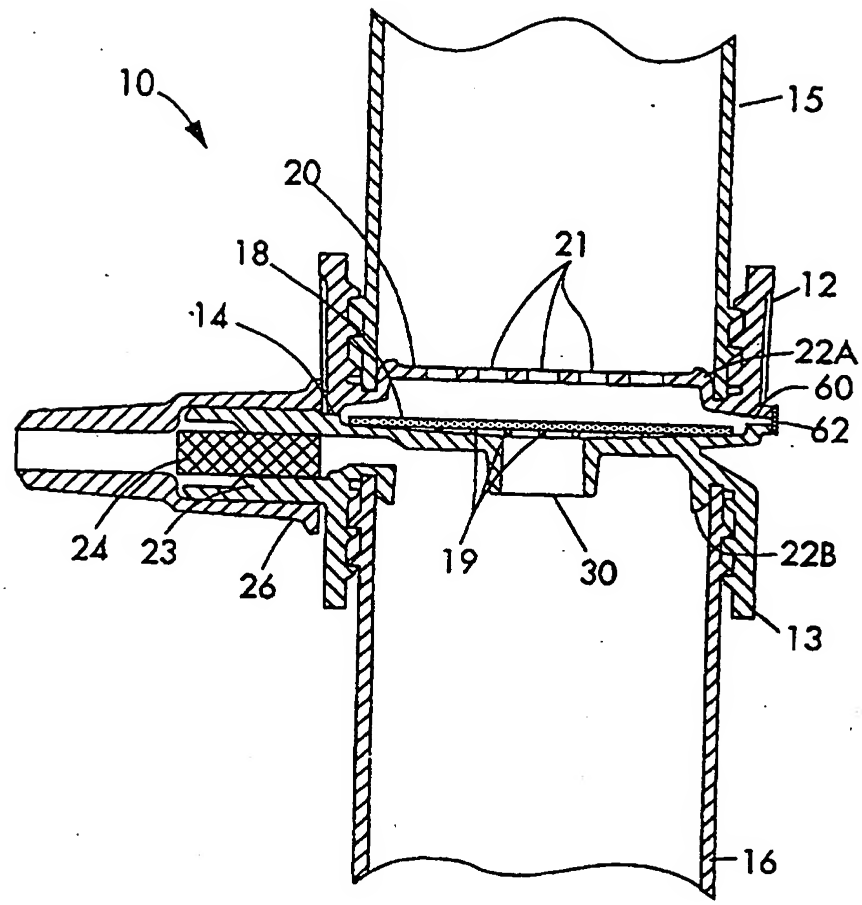

Fig. 5

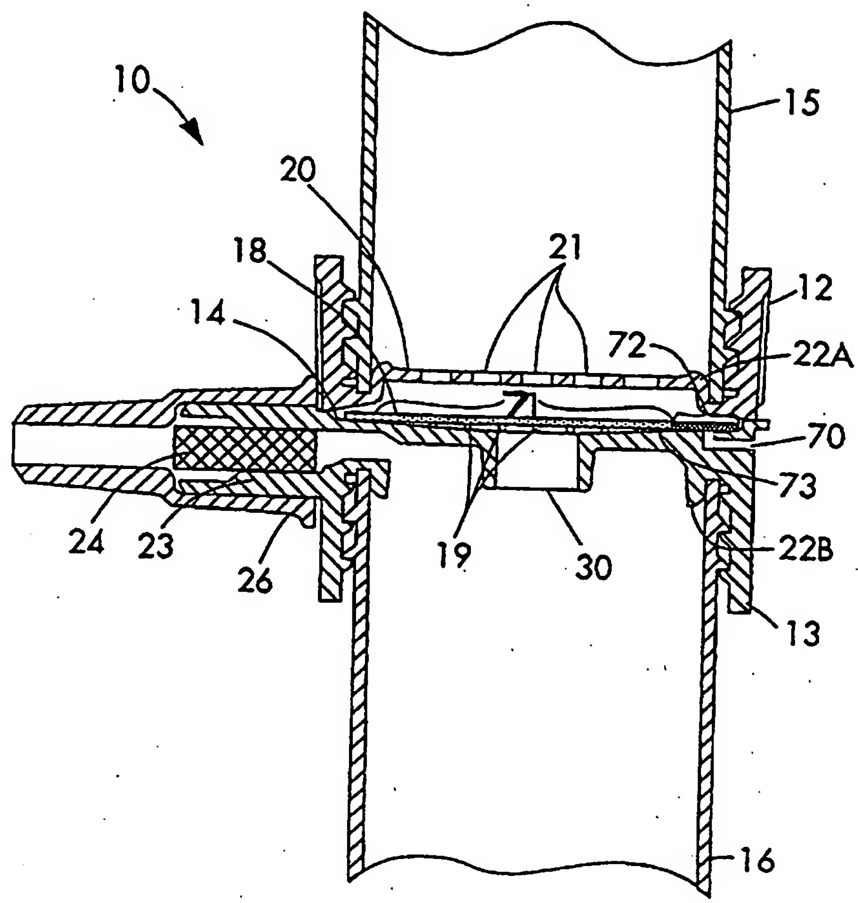

Fig. 6

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(73) Proprietor: **MILLIPORE CORPORATION**
80 Ashby Road
Bedford Massachusetts 01730 (US)

(72) Inventor: **Sarrasin, Michael J.**
24 New Castle Drive No 6
Nashua, NH 03060 (US)

(74) Representative: **Henkel, Feller, Hänzel & Partner**
Möhlstrasse 37
D-81675 München (DE)

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Description

This invention relates to a multi-well filtration device including a filtration membrane on each well which can be removed from the wells for analysis subsequent to filtration.

Test plates for in vitro analysis which contain a multiplicity of individual wells or reaction chambers are commonly known laboratory tools. Such devices have been employed for a wide variety of purposes and assays as exemplified by U.S. Patents 3,694,464; 4,304,865; 4,276,048; 4,154,795; 4,427,415; 4,526,690 and Re 30,562. Microporous membrane filters and filtration devices containing such microporous membranes have been especially useful with many of the recently developed cell and tissue culture techniques and assays, particularly those in the field of virology and immunology, wherein the material of interest is retained by the filter. Typically, a ninety-six well filtration plate is used to conduct multiple assays simultaneously, some steps which may last several hours prior to performing filtration. Often the material of interest is retained on the filter. However, if an analytical instrument of interest cannot read the filters directly in the plate wells, the filters must be removed from the wells.

It has also been proposed to utilize a die-punch having a flat face which is inserted into the well and through the filter paper bearing the retentate in order to direct the filter paper and retentate from the well into a vial for subsequent testing. This system has two major problems. First, many times only a portion of the filter paper circumference is sheared and the filter disc remains attached to the well. Secondly, the flat face of the punch tends to remove some of the retentate from the filter paper so that the subsequent testing is inaccurate. An alternative system utilizes a hollow tube as a punch to minimize the contact face of the punch and reduce the amount of sample accidentally transferred to the punch. In another system, the filter is scored about its circumference in order to facilitate subsequent punching. This system is undesirable since accidental rupturing of the filter paper along the scoring can occur. Also, all of these systems are undesirable since they each involve the physical transfer of individual filter discs.

For a counter which requires a flat sample array, it would be preferable to transfer the filter discs directly from the well ends to a film coated with adhesive to maintain the relative locations of all the filter discs. This system is satisfactory with some membrane filters but not with multi layer filter laminates which have a tendency to delaminate thereby effecting transfer of only a portion of the bottom filter layer to the adhesive and leaving the support web and all the upper filter surface and sample still attached to the well. Accordingly, it would be desirable to provide a means for removing retentate and filter paper from a multi-well filtration plate which assures that the filter paper will be completely removed from the well without loss of a portion of the retentate for purposes of subsequent testing. Furthermore, it would be desirable to provide such means which permits removal of the filter and retentate from a plurality of wells simultaneously onto a flat surface so that use of analytical apparatus requiring a flat surface for supporting samples is facilitated.

SUMMARY OF THE INVENTION

This invention provides a multi-well filtration apparatus suitable for the assay of microliter quantity of biological and biochemical materials. The filtration apparatus includes a plate having a plurality of wells, open at one end and having a filtration membrane positioned across an opposing end of each well. The filtration membrane can be formed as one layer or as a laminate and is shaped so that it can be easily removed from the bottom of the well after the exposed lower surface has been contacted with an adhesive sheet. The filtration membrane is shaped so that it can be heat sealed to the entire periphery , e.g., circumference of the well and has a tab section which extends outside of the seal periphery. The tab sections on each well extend in substantially the same direction so that after filtration, when an adhesive sheet is applied to the exposed lower surfaces of the filtration membranes to adhere them to the sheet, the membranes can be easily and completely torn away from the wells by pulling the sheet in a direction substantially opposite to the direction toward which the tab sections extend.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an expanded view of a vacuum assembly useful with the present invention.

Figure 2 is a top view of a filtration apparatus comprising a second plate portion of this apparatus.

Figure 3 is a cross sectional view of the apparatus of this invention, shown partially assembled.

Figure 4 is a top view showing a means for removing filter membranes after filtration.

Figure 5 is a top view showing removed filter membranes positioned on an adhesive sheet.

DETAILED DESCRIPTION OF SPECIFIC EMBODIMENTS

This invention provides an improved multi-well filtration apparatus including a plurality of membrane filters which permits the recovery of retentate on the membrane filters produced during filtration. Each membrane filter is formed of a shape so that it can be heat sealed at the bottom of the well and includes a tab section extending outside the periphery of the seal. The tab section on each membrane filter extends generally in the same direction so that when an adhesive sheet is applied to the exposed bottom surface of the membrane filters, the filters can be completely removed from the wells by applying a pulling force to the adhesive sheet in a direction generally opposite to the direction in which the tabs extend when sealed to the wells. In this manner, since nothing touches the filter surface which bears the retentate, loss of retentate is prevented and the retentates can be analyzed when positioned on a flat sheet.

Referring to Figure 1, a vacuum assembly is shown capable of simultaneously processing a plurality of test samples of a size usually up to about 400 microliters each. The vacuum assembly comprises a base 2 which acts as a vacuum chamber and contains hose barb 3 for connection to a regulated external vacuum source through hose 5. Positioned within the base 2 are liquid collection means 4 which includes a collection tray 6 and/or a receiving plate 8 having a plurality of individual chambers 9 for collecting filtrate. The individual chambers 9 are associated each with a single well 11 in filtration plate 12. A plate support 10 holding the filtration plate 12 above the fluid collection means 4 is separated by gaskets 14 and 16 which form an airtight seal in the presence of a vacuum force exerted through hose 5.

Referring to Figures 2 and 3, plate 12 includes a plurality of wells 11 to which are heat sealed filter membranes 15 including tab sections 17 which extend generally in the same direction. The filter membranes 15 are heat sealed on the lower surface 19 of well wall 21. Well 11 extends downwardly to the point such that membrane 15 is positioned above receptacle 9 such that the liquid passing through membrane 15 is directed into receptacle 9. Any conventional bonding method can be utilized to bond membrane 15 to plate 12. As shown, for example in Figure 3, the tab 17 can extend a distance outside the well 9 from the surface 19. However, it is to be understood that the tab can extend a distance which can be inside the well or to the well wall. In addition, the tab can extend from the entire periphery of the seal if desired. It is desirable to avoid a tab which is too narrow or which has an abrupt angle with the main disc in order to avoid tearing across the center portion of the disc rather than peeling. Representative suitable micro-porous membrane include nitrocellulose, cellulose acetate, polycarbonate, polypropylene and polyvinylidene fluoride microporous membranes. Alternatively, the membrane can comprise an ultrafiltration membrane, which membranes are useful for retaining molecules as small as about 100 daltons and generally molecules as large as about 2,000,000 daltons. Examples of such ultrafiltration membranes include polysulfone, polyvinylidene fluoride or cellulose or the like. Also, the membrane can be comprised of depth filter media such as paper or glass fibers. In addition, the filter membrane can be formed as a laminate structure comprising a microporous membrane bonded to a woven or non-woven substrate. The tab section of the membrane extends a distance between about 0.5 and about 5 mm, preferably about 0.2 mm from the line of sealing. When the major dimension or length of the tab section is too small, the membrane will have a high tendency to tear when removal from the wells 11 is attempted.

The membranes with the tab section can be formed by any conventional means such as by the steps of heat sealing a membrane sheet to the bottom surfaces of the wells 11 and then cutting the membrane sheet into the desired shapes such as by laser. Filtration then can be effected.

Referring to Figure 4, after filtration has been completed so that retentate is positioned on the membrane surfaces within wells 11, an adhesive sheet 25 is applied to the rententate-free bottom surface 23 of the membrane 15 so that both the filtrate sections and the tab section 17 of the membrane 15 are adhered to the sheet 25. The sheet 25 then is pulled in the direction of arrow 27 which is the direction about 180° from the direction in which the tab sections 17 extend. As shown in Figure 5, the membranes 15 including tab section 17 are adhered to the flat sheet 25 and the individual retentates thereon are exposed for analysis.

Claims

1. A filtration apparatus comprising:

   a plate (12) having a plurality of wells (11), having a first open end for introducing liquid into said well (11), a second end and an outside peripheral surface (19) about said second end,

   a filter membrane (15) bonded to said peripheral surface (19) of each well (11), said filter membrane (15) is shaped so that it can be sealed to the entire peripheral surface (19) and has a tab section (17) which extends outside of the seal periphery, all tab sections (17) extending the same direction so that after filtra-

tion, when an adhesive sheet (25) is applied to the exposed lower surfaces of the filtration membranes (15) to adhere them to the sheet (25), the membranes (15) can be easily and completely torn away from the wells (11) by pulling the sheet (25) in a direction (27) opposite to the direction toward which the tab sections (17) extend.

2. The apparatus of claim 1, wherein said filter membrane (15) is a microporous membrane.

3. The apparatus of claim 1, wherein said filter membrane (15) is an ultrafiltration membrane.

4. Tha apparatus of claim 1, wherein said filter membrane (15) is a depth filter.

5. The apparatus of claim 1, wherein said filter membrane (15) is a laminate.

Patentansprüche

1. Filtergerät, umfassend:
eine Platte (12) mit einer Vielzahl von Zellen (11), die ein offenes erstes Ende zum Einführen von Flüssigkeit in die Zelle (1.1), ein zweites Ende und eine um das zweite Ende herum angeordnete Außenumfangsfläche (19) aufweisen, (und)
eine mit der Umfangsfläche (19) jeder Zelle (11) (klebend) verbundene Filtermembran (15) einer solchen Form, daß sie mit der gesamten Umfangsfläche (19) versiegelt bzw. verklebt werden kann, und mit einem Laschenabschnitt (17), der vom Versiegelungsumfang nach außen ragt, wobei alle Laschenabschnitte (17) in der gleichen Richtung verlaufen, so daß dann, wenn nach der Filtration eine Klebefolie (25) an den freiliegenden Unterseiten der Filtermembranen (15) angebracht wird, um diese an der Folie (25) haften zu lassen, die Membranen (15) durch (Ab-)Ziehen der Folie (25) in einer Richtung entgegengesetzt zur Erstreckungsrichtung der Laschenabschnitte (17) leicht und vollständig von den Zellen (11) abziehbar sind.

2. Gerät nach Anspruch 1, wobei die Filtermembran (15) eine mikroporöse Membran ist.

3. Gerät nach Anspruch 1, wobei die Filtermembran (15) eine Ultrafiltrationsmembran ist.

4. Gerät nach Anspruch 1, wobei die Filtermembran (15) ein Tiefenfilter ist.

5. Gerät nach Anspruch 1, wobei die Filtermembran (15) ein Laminat ist.

Revendications

1. Appareil de filtration qui comprend:
   - un plateau (12) présentant une pluralité d'alvéoles (11) avec une première extrémité ouverte en vue de l'introduction d'un liquide dans ladite alvéole (11), une seconde extrémité fermée et une surface périphérique extérieure (19) autour de ladite seconde extrémité,
   - une membrane formant filtre (15) soudée à ladite surface périphérique (19) de chaque alvéole (11), ladite membrane formant filtre (15) ayant une forme telle qu'elle peut être scellée à toute la surface périphérique (19) et comprenant un morceau formant onglet (17) qui s'étend à l'extérieur de la périphérie scellée, tous les morceaux formant onglets (17) s'étendant dans la même direction si bien qu'après filtration, quand une feuille adhésive (25) est appliquée sur les surfaces inférieures dénudées des membranes de filtration (15) pour les faire adhérer à la feuille (25), les membranes peuvent être facilement et complètement arrachées des alvéoles (11) par traction de la feuille (25) dans la direction (27) opposée à celle dans laquelle s'étendent les morceaux formant onglets (17).

2. Appareil selon la revendication 1, dans lequel ladite membrane formant filtre (15) est une membrane microporeuse.

3. Appareil selon la revendication 1, dans lequel ladite membrane formant filtre (15) est une membrane d'ultra-filtration.

4. Appareil selon la revendication 1, dans lequel ladite membrane formant filtre (15) est un filtre de profondeur.

5. Appareil selon la revendication 1, dans lequel ladite membrane formant filtre (15) est un stratifié.

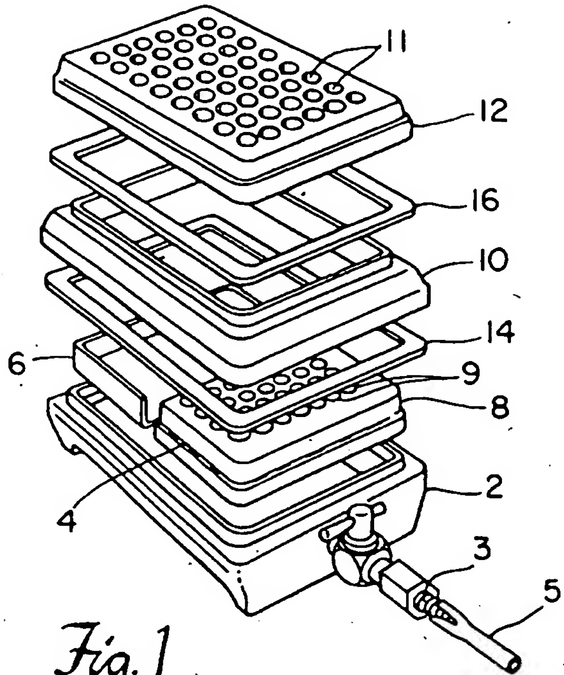

Fig. 1

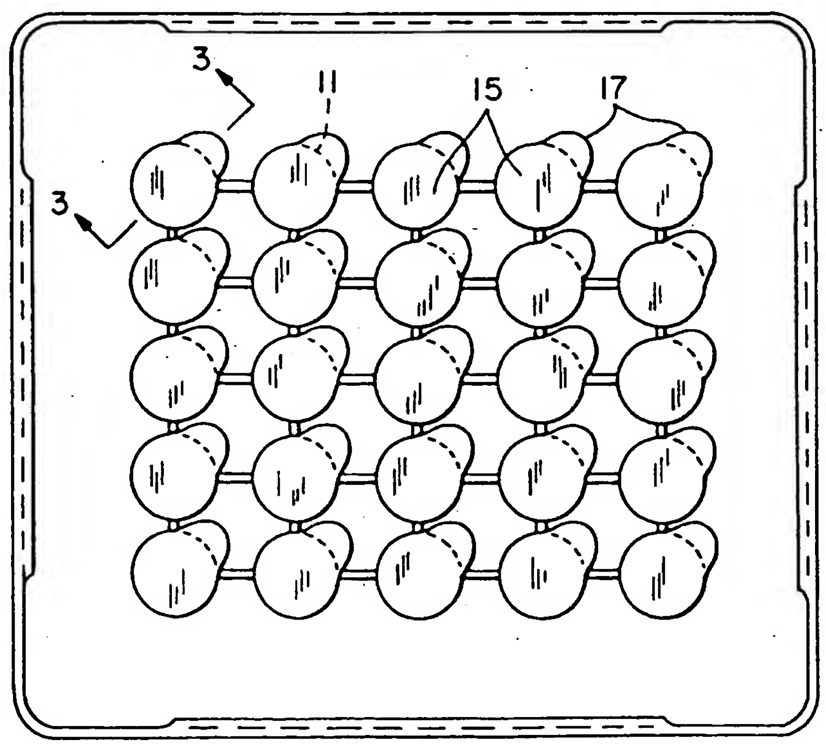

Fig. 2

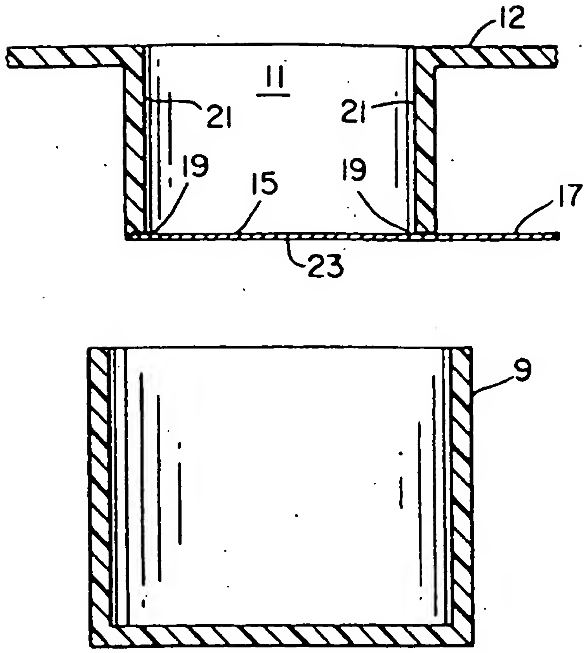

Fig. 3

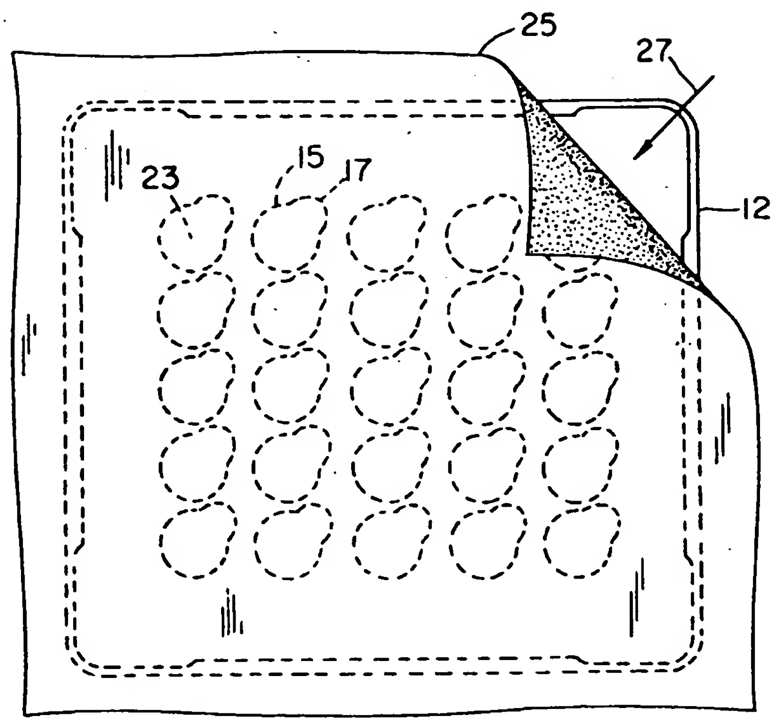

Fig. 4

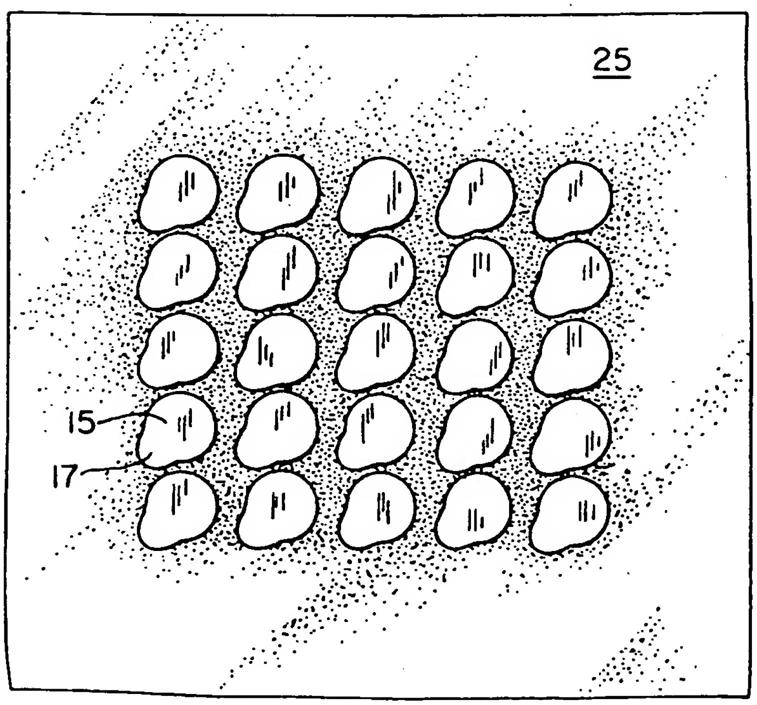

Fig. 5